DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Sharon L. Camp, Ph.D.
President and CEO
Women's Capital Corporation
1990 M Street, NW
Suite 250
Washington, DC 20036

RE: NDA 21-045
Plan B (levonorgestrel) Tablets, 0.75 mg
MACMIS ID # 11214

Dear Dr. Camp:

This letter concerns Women's Capital Corporation's (WCC) direct-to-consumer (DTC) broadcast and print advertisements (ads) for Plan B (levonorgestrel) Tablets for emergency contraception. These ads were disseminated by radio broadcast (60 second "Jane's Lucky Day") airing on selected Seattle, Washington radio stations and by publication as a full-page print ad ("'Oops' and 'Uh-oh'") appearing in the *Seattle Weekly*. The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed these ads as part of its monitoring and surveillance program.

DDMAC has concluded that WCC's ads are false, lacking in fair balance, or otherwise misleading in violation of the Federal Food, Drug, and Cosmetic Act (Act) and applicable implementing regulations. Specifically, the DTC radio and print ads overstate efficacy, fail to convey important limitations on use, and minimize important information about risks associated with the use of Plan B Tablets emergency contraception. As a result, the ads raise significant public health and safety concerns.

Background

Plan B is an emergency contraceptive prescription drug product approved to prevent pregnancy after unprotected sex, such as intercourse without contraception or when a contraceptive fails. Plan B is approved "for emergency use, and should not be used in place of regular contraception since it is not as effective as regular contraceptives." (See Plan B approved patient labeling). Similarly, a Bolded Warning in the Plan B approved physician labeling (PI) states: "Plan B is not recommended for routine use as a contraceptive...." The Clinical Trials section of the PI also states that "[e]mergency contraceptives are not as effective as routine contraception." Moreover, the PI stresses that, "[t]o obtain optimal efficacy," (the greatest likelihood of preventing an unintended pregnancy), "the first tablet should be taken as soon as possible within 72 hours of intercourse. The second tablet must be taken 12 hours later." (emphasis added) (See the Indications & Usage and Dosage and Administration sections)

A patient considering use of Plan B emergency contraception should be informed not only of these limitations on efficacy, and the importance of using the product promptly, but also of the potential risks associated with use of the product. A patient needs to be informed that she should not use Plan B if she has unexplained vaginal bleeding or if she is already pregnant, and that Plan B does not protect against HIV infection (AIDS) or other sexually transmitted diseases (STDs). She must also be aware that severe abdominal pain can signal the possibility of a serious medical condition (i.e., tubal (ectopic) pregnancy) requiring immediate medical intervention.

False or Misleading Efficacy Presentations – Overstatement of Efficacy

Prescription drug ads are false or misleading if they suggest that a prescription drug is more effective than has been demonstrated by substantial evidence or substantial clinical experience (21 CFR 202.1(e)(6)(i)). The totality of claims and presentations in the radio and print ads misleadingly overstates the efficacy of Plan B. The radio ad claims that "[I]t's Jane's lucky day, all right. Because she still has 72 hours after unprotected sex to prevent pregnancy with Plan B emergency contraception. Similarly, the print ad claims, "Find out how Plan B, taken within 72 hours of intercourse, can be your back-up plan in preventing pregnancy. And find yourself uttering phrases like 'Phew!'" These unqualified characterizations suggest that Plan B is guaranteed to prevent the risk of unintended pregnancy every time, and they also fail to convey that Plan B is for emergency use only because Plan B is not as effective as routine contraceptives.

Specifically, statements such as "she still has 72 hours after unprotected sex to prevent pregnancy" and "Taken within 72 hours of intercourse" misleadingly suggest that a woman could take Plan B as late as three days after unprotected intercourse with the same likelihood of reducing the risk of unintended pregnancy. Thus, the ads fail to clearly communicate a crucial limitation to the effective use of Plan B, that it must be used as soon as possible. By presenting the 72 hour limitation as a product benefit rather than a limitation to its use, the Plan B ads fail to adequately convey, and indeed undermines, this crucial efficacy-related prescribing information.

Furthermore, the radio and print ads are misleading because they do not clearly communicate the indication and limitation of use for Plan B as emergency contraception after unprotected sex. The ads omit context and therefore minimize material facts in light of representations made about preventing unintended pregnancy by failing to explain that Plan B is for emergency use only because it is less effective than routine contraception methods. Without this important contextual information, women may be misled into believing that, contrary to the approved labeling, Plan B can be used for routine contraception.

Minimization of Important Risk Information

The Act requires that all prescription drug advertisements include a true statement of information in brief summary relating to side effects, contraindications (including warnings, precautions, etc.), and effectiveness (21 U.S.C. 352(n)), commonly referred to as the "brief summary." However, the regulations distinguish print ads from broadcast ads in fulfillment of the "brief summary" requirement (21 CFR 202.1(e)(1)). Print ads must present a brief summary, which contains each specific side effect and contraindication from the product's approved labeling (PI). Ads broadcast through media,

such as television or radio, are required to contain a brief summary or, alternatively, make "adequate provision" for the dissemination of the PI in connection with the broadcast presentation. The regulations also require that broadcast ads include information relating to the major side effects and contraindications of the advertised drug in either the audio or audio and visual parts of the broadcast presentation, commonly referred to as the "major statement." The content and presentation of the radio and print ads misleadingly minimize or omit important risk information. Consequently, the ads misleadingly suggest that Plan B is safer than has been demonstrated by substantial evidence or substantial clinical experience (21 CFR 202.1(e)(6)(i)).

Radio Ad

The radio ad directive "Call your doctor right away if you have severe abdominal pain" fails to provide sufficient context to explain that it is important that the woman contact her doctor immediately because severe abdominal pain may signal a serious medical condition, i.e., a tubal (ectopic) pregnancy, which can be life-threatening. Furthermore, the radio ad fails to disclose the significant public health message included in the Precautions section of the PI that Plan B will not protect against HIV infection (the virus causing AIDS) or any other sexually transmitted disease. Accordingly, this should be included as part of the "major statement."

The radio ad also fails to present the information relating to major side effects and contraindications (including warnings and precautions) with a prominence and comprehension reasonably comparable with the effectiveness claims in the ad (21 CFR 202.1(e)(7)(viii)). The faster pacing of the announcer audio presenting the risk information (as is explicitly directed by the script, "faster") is read at a speed at which the risk information is not likely to be understood, much less comprehended, by the typical consumer. Moreover, the description of the most serious risks associated with use of Plan B is not as audible or as well articulated as the effectiveness audio presentation. Therefore, the ad is misleading because of this unbalanced presentation of effectiveness versus serious risk information.

Print Ad

The print ad lacks fair balance and is misleading because it fails to present information about the risks associated with the use of Plan B with a prominence and readability reasonably comparable to the presentation of information relating to the effectiveness of the drug, taking into account all implementing factors (21 CFR 202.1(e)(7)(viii)).

The only risk information included in the one-page print ad is presented on the bottom half of the newspaper page as an accompanying "brief summary" of risk information. By contrast, effectiveness claims like "Phew! ACCIDENTS HAPPEN. That's why there's Plan B." are presented in much larger type and highlighted in a box. The presentation of risk information in very small type across three columns is not reasonably comparable, in either readability or prominence, to the ad's presentation of Plan B's effectiveness. Furthermore, the print ad conveys the effectiveness information in consumer-friendly language, but does not convey the risk information in comparably consumer-friendly language. Therefore, the ad is misleading because of this unbalanced presentation of product benefits versus risk information.

Failure to Disclose Established Drug Name

The print and radio ads fail to disclose the established drug name (levonorgestrel) in the ad. Prescription drug ads are required to include the established drug name (21 USC 352 (n)).

Failure to Make Adequate Provision for Dissemination of the PI

The prescription drug advertising regulations require sponsors of broadcast ads to present a brief summary or, alternatively, make "adequate provision ... for dissemination of the approved or permitted package labeling in connection with the broadcast presentation" (21 CFR 202.1(e)(1)).

The Plan B radio ad does not contain a brief summary. Consequently, the regulations require that adequate provision be made for dissemination of the (PI) in connection with the ad. The radio ad states, "To find a pharmacist in Washington who provides Plan B, call 1-866-TURN TO PLAN B or visit www dot go to plan b dot com. For more information, see our ad in the *Seattle Weekly*." The statement "To find a pharmacist in Washington who provides Plan B, call....or visit www...." (emphasis added), fails to clearly communicate that the telephone number, website address, and pharmacist are ways to access the approved product labeling and additional product information.

Conclusions and Requested Actions

WCC should immediately cease dissemination and distribution of these and other similar promotional materials for Plan B that contain the same or similar claims or presentations. Please submit a written response to DDMAC on or before December 4, 2002, describing your intent and plans to comply with the above. In its letter to DDMAC, WCC should include the date on which these and other similarly violative materials were discontinued.

WCC should direct its response to the undersigned by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications HFD-42, Rm. 8B-45, 5600 Fishers Lane, Rockville, Maryland 20857. In all future correspondence on this matter, please refer to MACMIS ID# 11214 as well as the NDA number. DDMAC reminds WCC that only written communications are considered official.

Sincerely,

{See appended electronic signature page}

Joan Hankin
Consumer Promotion Analyst
Division of Drug Marketing,
Advertising, and Communications

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Joan Hankin
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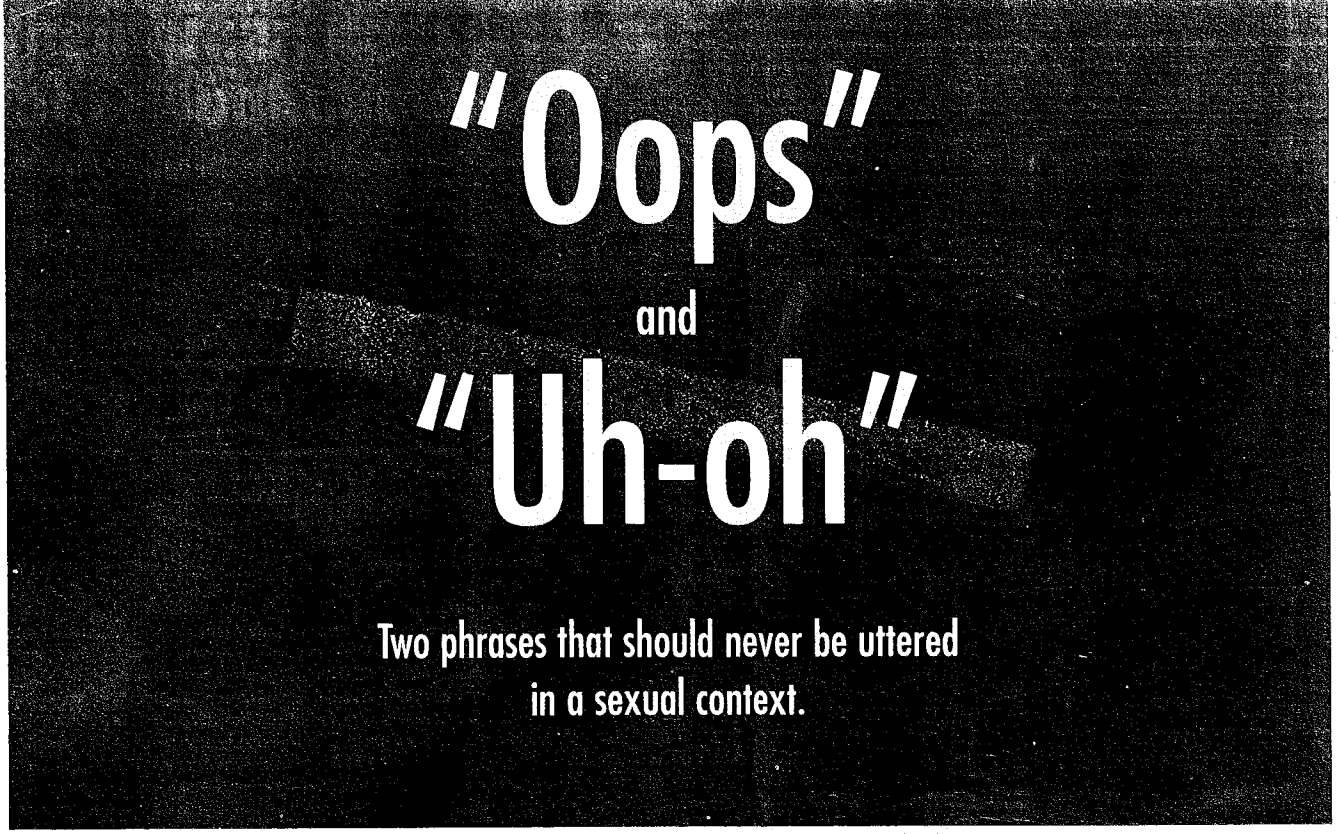

Find out how Plan B®, taken within 72 hours of intercourse, can be your back-up plan in preventing pregnancy. And find yourself uttering phrases like "Phew!" ACCIDENTS HAPPEN. That's why there's Plan B®. To learn more, visit www.go2planB.com or call 1-866-Turn2planB.

PLAN B® (LEVONORGESTREL) TABLETS, 0.75 mg

Plan B® is intended to prevent pregnancy after known or suspected contraceptive failure or unprotected intercourse. Emergency contraceptive pills (like all oral contraceptives) do not protect against infection with HIV (the virus that causes AIDS) and other sexually transmitted diseases.

Special Populations

This product is not intended for use in geriatric (age 65 years or older) populations and pharmacokinetic data are not available for this population.

This product is not intended for use in pediatric (premenarchal) populations, and pharmacokinetic data are not available for this population.

No formal studies have evaluated the effect of race. However, clinical trials demonstrated a higher pregnancy rate in the Chinese population. The reason for this apparent increase in the pregnancy rate of emergency contraceptives in Chinese women is unknown.

No formal studies have evaluated the effect of hepatic insufficiency or renal insufficiency on the disposition of emergency contraceptive tablets.

INDICATIONS & USAGE

Indication

Plan B® is an emergency contraceptive that can be used to prevent pregnancy following unprotected intercourse or a known or suspected contraceptive failure. To obtain optimal efficacy, the first tablet should be taken as soon as possible within 72 hours of intercourse. The second tablet must be taken 12 hours later.

Clinical Studies

A double-blind, controlled clinical trial in 1,955 women compared the efficacy and safety of Plan B® (one 0.75 mg tablet of levonorgestrel taken within 72 hours of intercourse, and one tablet taken 12 hours later) to the Yuzpe regimen (two tablets of 0.25 mg levonorgestrel and 0.05 mg ethinyl estradiol). Plan B® was at least as effective as the Yuzpe regimen in preventing pregnancy. After a single act of intercourse, the expected pregnancy rate of 8% (with no contraception) was reduced to approximately 1% with Plan B®. Thus, Plan B® reduced the expected number of pregnancies by 89%.

Emergency contraceptives are not as effective as routine contraception since their failure rate, while low based on a single use, would accumulate over time with repeated use (see Warnings).

CONTRAINDICATIONS

Progestin-only contraceptive pills (POPs) are used as a routine method of birth control over longer periods of time, and are contraindicated in some conditions. It is not known whether these same conditions apply to the Plan B® regimen consisting of the emergency use of two progestin pills. POPs however, are not recommended for use in the following conditions:

- Known or suspected pregnancy
- Hypersensitivity to any component of the product
- Undiagnosed abnormal genital bleeding

WARNINGS

Plan B® is not recommended for routine use as a contraceptive.

Plan B® is not effective in terminating an existing pregnancy.

Effects on Menses

Menstrual bleeding patterns are often irregular among women using progestin-only oral contraceptives and in clinical studies of levonorgestrel for postcoital and emergency contraceptive use. Some women may experience spotting a few days after taking Plan B®. At the time of expected menses, approximately 75% of women using Plan B® had vaginal bleeding similar to their normal menses, 12-13% bled more than usual, and 12% bled less than usual. The majority of woman (87%) had their next menstrual period at the expected time or within ± 7 days, while 13% had a delay of more than 7 days beyond the anticipated onset of menses. If there is a delay in the onset of menses beyond 1 week, the possibility of pregnancy should be considered.

Ectopic Pregnancy

Ectopic pregnancies account for approximately 2% of reported pregnancies (10.7 per 1,000 reported pregnancies). Up to 10% of pregnancies reported in clinical studies of routine use of progestin-only contraceptives are ectopic. A history of ectopic pregnancy need not be considered a contraindication to use of Plan B®. Users, however, should be alert to the possibility of an ectopic pregnancy if severe lower abdominal pain occurs.

PRECAUTIONS

Pregnancy

Many studies have found no effects on fetal development associated with long-term use of contraceptive doses of oral progestins (POPs). The few studies of infant growth and development that have been conducted with POPs have not demonstrated significant adverse effects.

STD/HIV

Plan B®, like progestin-only contraceptives, does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

Physical Examination and Follow-Up

A physical examination is not required prior to using Plan B®. A follow-up physical or pelvic examination, however, is recommended if there is more than one week of delay in the next menstrual period or if the user has any concerns after taking Plan B®.

Carbohydrate Metabolism

The effects of Plan B® on carbohydrate metabolism are unknown. Some users of progestin-only oral contraceptives (POPs) may experience slight deterioration in glucose tolerance, with increases in plasma insulin; however, women with diabetes mellitus who use POPs do not generally experience changes in their insulin requirements. Nonetheless, diabetic women should be monitored while taking Plan B®.

Nursing Mothers

Small amounts of progestin pass into the breast milk in women taking progestin-only pills for long-term contraception resulting in steroid levels in infant plasma of 1-6% of the levels of maternal plasma. However, no adverse effects due to progestin-only pills have been found on breastfeeding performance, either in the quality or quantity of the milk, or on the health, growth or development of the infant.

Pediatric Use

Safety and efficacy of progestin-only pills have been established in women of reproductive age for long-term contraception. Safety and efficacy are expected to be the same for postpubertal adolescents under the age of 16 and for users 16 years and older. Use of Plan B® emergency contraception before menarche is not indicated.

Fertility Following Discontinuation

The limited available data indicate a rapid return of normal ovulation and fertility following discontinuation of progestin-only pills for emergency contraception and long-term contraception.

ADVERSE REACTIONS

The most common adverse events in the clinical trial for women receiving Plan B® included nausea (23%), abdominal pain (18%), fatigue (17%), headache (17%), and menstrual changes. The table below shows those adverse events that occurred in ≥ 5% of Plan B® users.

Adverse Events in ≥ 5% of Women, by % Frequence

Most Common Adverse Events	Plan B® Levonorgestrel N=977 (%)
Nausea	23.1
Abdominal pain	17.6
Fatigue	16.9
Headache	16.8
Heavier menstrual bleeding	13.8
Lighter menstrual bleeding	12.5
Dizziness	11.2
Breast tenderness	10.7
Other complaints	8.7
Vomiting	5.6
Diarrhea	5.0

Plan B® demonstrated a superior safety profile over the Yuzpe regimen for the following adverse events:

- *Nausea:* Occurred in 23% of women taking Plan B® (compared to 50% with Yuzpe)
- *Vomiting:* Occurred in 6% of women taking Plan B® (compared to 19% with Yuzpe)

OVERDOSAGE

There are no data on overdosage of Plan B®, although the common adverse event of nausea and its associated vomiting may be anticipated.

DOSAGE AND ADMINISTRATION

One tablet of Plan B® should be taken orally within 72 hours after unprotected intercourse. The second tablet should be taken 12 hours after the first dose. Efficacy is better if Plan B® is taken as directed as soon as possible after unprotected intercourse. Plan B® can be used at any time during the menstrual cycle.

The user should be instructed that if she vomits within one hour of taking either dose of medication she should contact her health care professional to discuss whether to repeat that dose.

HOW SUPPLIED

Plan B® (levonorgestrel) tablets, 0.75 mg are available for a single course of treatment in PVC/aluminum foil blister packages of two tablets each. The tablet is white, round, and marked: INOR.

Store Plan B® tablets at 25°C (77°F); excursions permitted to 15 – 30°C (59 – 86°F). Plan B® is distributed by the Women's Capital Corporation, 1990 M Street, NW, Washington, DC 20036.

Rx Only

Radio

Women's Capital Corp.
Plan B Radio :60
WCR PHM D30386
"Jane's Lucky Day"
AS-PRODUCED
ISCI # ZDNK-6982

MUSIC: *skippy bossa nova or samba (under)*

ANNOUNCER: Today is Jane's lucky day. First, she went to get her haircut.

SFX: snip, snip, snip

HAIRDRESSER: Oops.

JANE: Did you say oops?

HAIRDRESSER: Did you say bald?

JANE: I said a bob.

HAIRDRESSER: Oops.

ANNOUNCER: Then, Jane went to see the dentist.

DENTIST: A little suction here. (***SFX:*** *gargle-y suction sound*) A drill. (SFX: *VRRR! VRRR!)* Woopsadaisy. (silence)

JANE: (*with mouth full of cotton*) Eth-yooz me, thoctor? Did you thay woopthedaisy.

ANNOUNCER: Then. Jane went home and had a romantic night with her boyfriend.

MAN: Oh, yeah...

JANE: Oh, oh...

MAN: Uh-oh.

JANE: Oh no.

ANNOUNCER: Yes, it's Jane's lucky day, all right. Because she still has 72 hours after unprotected sex to prevent pregnancy with Plan B emergency contraception. To find a pharmacist in Washington who provides Plan B, call 1-866-TURN TO PLAN B or visit www dot go to plan b do com. For more information, see our ad in the *Seattle Weekly*.

ANNOUNCER (faster): Plan B is not recommended for routine contraception and won't work if you're already pregnant. Common side effects include nausea, abdominal pain and fatigue. Women with unexplained vaginal bleeding should not use Plan B. Call your doctor right away if you have severe abdominal pain. A pharmacist or healthcare provider can help you decide if Plan B is right for you.